NAGKC Project: Multi-Institutional Retrospective Analyses of Stereotactic Radiosurgery For Hemangiopericytoma

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Abstract
Intracranial hemangiopericytoma is a rare CNS tumor that exhibits a high incidence of local recurrence and remote metastasis. Radiosurgery has emerged as an alternative approach to microsurgery. Retrospective analyses of outcomes following stereotactic radiosurgery for hemangiopericytoma have been published. The case numbers in each series are usually less than 30 patients. The precise indication and timing of radiosurgery are ill defined for this rare tumor type. The purpose of this multi-center project is to evaluate the role of Gamma Knife surgery (GKS) in the management of intracranial hemangiopericytomas.

Keyword: cavernous sinus hemangioma, stereotactic radiosurgery, gamma knife radiosurgery, cavernous sinus
**Background**

Hemanigopericytoma is a rare, WHO grade II vascular neoplasm. Although they share similar radiographic features with intracranial meningiomas, they tend to have higher rate of local and distal recurrence than WHO grade I meningiomas. In addition, because they are true vascular neoplasms, the operative mortality rates between 9-24%, especially when they are located at the skull base. Microsurgical approach is the only way to cure, however, a gross-total resection was associated with almost 100% recurrence. However, resection may result in severe bleeding and even operative mortality. Based on the characteristics of the hemangiopericytoma mentioned above, the role of adjuvant therapy is important.

Radiosurgery can achieve a steep dose gradient that minimizes the radiation delivered to the surrounding areas. Consequently, it is possible to deliver a significantly larger and more biological effective dose to the tumor and minimize other undesired side effects of radiotherapy. Because of the nature of invasiveness and distal metastasis of the hemangiopericytoma, upfront or salvage radiation therapy for residual tumor are suggested in some series. (see Table below)

For the experience of radiosurgery for highly-vascular tumors, such as glomus tumors and cavernous sinus cavernous hemangiomas, SRS often shows benefit in remarkable effect on tumor control. It can also help reduce tumor size and vascularity to facilitate subsequent total removal by microsurgery. SRS should be a good treatment alternative, either as an upfront or salvage therapy for residual hemangiopericytomas. Since 1993, 10 more reports have been published, mostly showing good response. However, they usually reported a small number of patient population, usually no more than 30. In most reports, radiosurgery is used as adjuvant therapy after partial tumor removal. Therefore, we propose the project to evaluate the role of Gamma Knife surgery (GKS) in the management of intracranial hemangiopericytomas via multicenter data pooling.

**Specific aim**

The purpose of this study is to clarify the efficacy and safety of SRS on the treatment of hemangiopericytomas. Prognostic factors will be analyzed for better prediction of treatment outcomes. To further investigate the role of Gamma Knife surgery (GKS) in treating hemangiopericytomas.

**Importance**

1. Define the efficacy of SRS for hemangiopericytomas
2. Define the complications of SRS for hemangiopericytomas
3. Analyze the prognostic factors for better radiosurgical outcomes.
4. Establish the role of radiosurgery in treating hemangiopericytomas

**Related publications**

Since 1993, Coffey et al. reported on 5 patients with 11 tumors treated with GKS. They demonstrated dramatic shrinkage of 9 lesions after a mean follow-up of 14.8 months. Galanis et al. added 5 more patients to the series by Coffey et al., for a total of 20 hemangiopericytomas, with a longer mean follow-up period of 6-36 months. Fourteen of the hemangiopericytomas decreased in size, 4 disappeared radiographically, and 2 were stable in size. The margin doses ranged from 12-18 Gy in both series. Payne et al. demonstrated 10 patients with 12 tumors treated by GKS with mean margin dose of 14Gy. Nine tumors decreased in size and 3 remained stable in a mean follow-up of 24.8 months. Sheehan et al. reviewed 14 patients with 15 hemangiopericytomas at UPMC, and showed the 5-year local tumor control rate and survival were 76 and 100%, respectively, under margin dose of 11-20 Gy. Despite this high local control rate, remote metastases developed in 29% of the patients, indicating that local tumor control afforded by radiosurgery provided seemingly
little protection from distant metastatic spread. Moreover, the author found repeat radiosurgery for lesions for which initial radiosurgery failed offered <6 months of tumor control.

Chang and Sakamoto\textsuperscript{1} described 8 patients who had undergone LINAC-based radiosurgery. After a mean FU of 44 months, 6 tumors decreased in size, but 2 progressed in last FU. Ecker et al.\textsuperscript{3} reported on 15 patients harboring 45 lesions who underwent GKS with mean margin dose of 16Gy, 42 of 45 tumors had controlled, either shrinkage or cease growing. Kano et al.\textsuperscript{7} Reviewed the cases of 20 patients who had undergone GKS for 29 tumors. They reported a median FU of 62.6 months result, showing four patients died of dissemination throughout the neuraxis and 1 died of liver and lung metastases. Three patients developed local tumor progression ad died. The tumor control rate was 72.4\% (n=21/29). The last but not the least, Olson et al.\textsuperscript{13} used the database at UVA to demonstrate 47.6\% local tumor control rate at median follow-up of 68 months, which is the longest follow-up in current literature. The actual progression-free survival rates were 90, 60.3, and 28.7\% at 1, 3, 5 years after initial GKS. The actual progression-free survival rates improved to 95, 71.5, and 71.5\% at 1, 3, 5 years after multiple GKS treatments. The 5-year survival rate was 81\%.

**Data Collection:** The spreadsheet excel file is also attached. Data Collection will include but not limited to the following. Age, Sex, Clinical Symptoms, Presenting neurological deficits, Prior treatment for the lesions, Prior hemorrhage, Dose of radiation (Gy), Dose planning, Tumor location, Number of months after radiosurgery, Tumor size (cc), Post intervention complications, Follow up symptoms, Follow up-brain imaging (Tumor Size), Follow up- brain edema, Number of months until of tumor progression, Follow-up of additional treatment (surgical resection, radiation, radiosurgery), follow up duration, Progression free survival, Distance metastasis.

**Statistical Analysis:** We will construct Kaplan-Meier plots for progression-free survival. Progression-free survival will be calculated from the day of the first neurosurgical intervention using the Kaplan-Meier method. Univariate analysis will be performed on the Kaplan-Meier curves using log rank statistic with p < 0.05 set as significant. We will also analyze the prognostic factor using multivariate analysis (Cox proportional hazards model or logistic proportional hazards model). Standard statistical processing software (SPSS, version 15.0 and Prism, version 4.0) will be used.
Table. Series of GKS in patients with hemangiopericytomas

<table>
<thead>
<tr>
<th>Author, year</th>
<th>No. patients/tumors</th>
<th>Margin dose (Gy)</th>
<th>FU (months)</th>
<th>Tumor control at last FU (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffey, 1993</td>
<td>5/11</td>
<td>15.5</td>
<td>14.8</td>
<td>81.8</td>
</tr>
<tr>
<td>Falanis, 1998</td>
<td>10/20</td>
<td>12-18</td>
<td>6-36</td>
<td>NA</td>
</tr>
<tr>
<td>Payne, 2000</td>
<td>10/12</td>
<td>14</td>
<td>24.8</td>
<td>75</td>
</tr>
<tr>
<td>Sheehan, 2002</td>
<td>14/15</td>
<td>15</td>
<td>31.3</td>
<td>79</td>
</tr>
<tr>
<td>Chang, 2003</td>
<td>8/8</td>
<td>20.5</td>
<td>44</td>
<td>75</td>
</tr>
<tr>
<td>Ecker, 2003</td>
<td>14/45</td>
<td>16</td>
<td>45.6</td>
<td>93</td>
</tr>
<tr>
<td>Kano, 2008</td>
<td>20/29</td>
<td>15</td>
<td>37.9</td>
<td>72.4</td>
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<tr>
<td>Oslo, 2010</td>
<td>21/28</td>
<td>17</td>
<td>69</td>
<td>46.4</td>
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</table>
